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BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte JOSEPH FISHER, JAMES LORENS,
DONALD PAYAN, and ALEXANDER ROSSI

Appeal 2009-015210
Application 09/293,670
Technology Center 1600

Before DEMETRA J. MILLS, FRANCISCO C. PRATS, and
MELANIE L. McCOLLUM, *Administrative Patent Judges*.

PRATS, *Administrative Patent Judge*.

DECISION ON APPEAL[1]

This appeal under 35 U.S.C. § 134 involves claims to methods of screening cells. The Examiner rejected the claims as obvious.

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[1] The two-month time period for filing an appeal or commencing a civil action, as recited in 37 C.F.R. § 1.304, or for filing a request for rehearing, as recited in 37 C.F.R. § 41.52, begins to run from the "MAIL DATE" (paper delivery mode) or the "NOTIFICATION DATE" (electronic delivery mode) shown on the PTOL-90A cover letter attached to this decision.

We have jurisdiction under 35 U.S.C. § 6(b). We affirm.

STATEMENT OF THE CASE

Claims 17-26, 30, and 32 stand rejected and are on appeal (App. Br. 3).[2] Claim 17, the only independent claim, is representative and reads as follows:

> 17. A method of screening for an alteration in cellular phenotype, said method comprising:
>
> a) providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents;
>
> b) sorting said population of cells based on at least five parameters using fluorescence activated cell sorting (FACS); and
>
> c) detecting at least one cell of said population having said alteration in said cellular phenotype;
>
> wherein said cellular phenotype is selected from a group of cellular phenotypes consisting of cell cycle, apoptosis, exocytosis, expression of a cell surface receptor, and expression of a receptor protein.

The Examiner cites the following documents as evidence of unpatentability:

Uhr	US 5,612,185	Mar. 18, 1997
Nolan	WO 97/27212	Jul. 31, 1997

Tao Jia-ping et al., *Multi-parameter sorting technique in flow cytometry*, 17 CHINESE JOURNAL OF PHYSICAL MEDICINE 168-171 (1995).

E. Conneally et al., *Rapid and Efficient Selection of Human Hematopoietic Cells Expressing Murine Heat-Stable Antigen as an Indicator of Retroviral-Mediated Gene Transfer*, 87 BLOOD 456-464 (1996).

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[2] Appeal Brief filed May 7, 2008.

Izumi Hide et al., *Degranulation of Individual Mast Cells in Response to Ca^{2+} and Guanine Nucleotides: An All-or-None Event*, 123 THE JOURNAL OF CELL BIOLOGY 585-593 (1993).

The following rejections are before us for review:

(1) Claims 17-24 and 30, rejected under 35 U.S.C. § 103(a) as obvious over Uhr and Conneally (Ans. 4-7);

(2) Claims 17-25, 30, and 32, rejected under 35 U.S.C. § 103(a) as obvious over Nolan, Jia-ping, and Uhr (Ans. 7-10); and

(3) Claim 26, rejected under 35 U.S.C. § 103(a) as being unpatentable over Nolan, Jia-ping, Uhr, Hide, and Appellants' admitted prior art (Ans. 10-11).

OBVIOUSNESS -- UHR AND CONNEALLY

ISSUE

The Examiner finds that "Uhr, alone, discloses or teaches all the elements of the claim[ed] method. Uhr does not positively teach [a] library of retroviral vectors albeit, at least suggests said library of retroviral vectors" (Ans. 6).

To supplement the asserted suggestion in Uhr of using a library of retroviral vectors, however, the Examiner cites Conneally as teaching "the advantages in the use of recombinant retroviuses [sic] for the genetic modification of cells," the advantages including "the ability to assess gene transfer to specific subpopulations of cells immediately after infection. The detectable level is sorted by FACS" (*id.* at 6-7).

Based on these advantages, the Examiner concludes that the "use of recombinant retroviral vectors to transfect cells would have been obvious to

one having ordinary skill in the art at the time the invention was made as taught by Conneally and at least contemplated by Uhr" (*id.* at 7).

"In a nutshell, the Appellants submit that the claims are not obvious in view of the cited references because neither of the cited references provide a library of retroviral vectors" (App. Br. 5). Specifically, Appellants argue, the portion of Uhr cited by the Examiner to meet that feature, column 22, lines 14-20, only teaches inducing cell cycle arrest in tumor cells using gene therapy (*id.* at 6), and Conneally fails to remedy that shortcoming (*id.* at 7).

The Examiner responds that column 22 of Uhr teaches that the gene therapy may be effected using retroviruses (Ans. 11), and also teaches that cells may be transfected with at least two genes, c-fos and c-jun (*id.* at 13). Thus, the Examiner reasons, because the Specification defines "'library of cells'" as meaning "at least two cells", the claims encompass the process suggested by Uhr (*id.* at 13-14).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether the evidence of record supports the Examiner's finding that the cited references suggest a process that includes a step of "providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents" as recited in claim 17.

FINDINGS OF FACT ("FF")

Claims and Specification

1. Claim 17 recites a method of screening for an alteration in cellular phenotype. The method's first step is "(a) providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents."

2. The Specification states that, "[b]y a 'population of cells' or 'library of cells' or 'plurality of cells' herein is meant at least two cells, with at least about 10^3 being preferred, at least about 10^6 being particularly preferred, and at least about 10^8 to 10^9 being especially preferred" (Spec. 9).[3]

The Prior Art

3. Uhr discloses "strategies for the treatment of cancer, including methods to induce or maintain a state of arrest to prevent tumor growth or metastasis" (Uhr, col. 2, ll. 62-65).

4. In one embodiment Uhr discloses that "it is contemplated that tumor cell cycle arrest may be induced by gene therapy. DNA encoding key genes in this process, such as, for example, c-fos or c-jun, may be applied directly to cells, in the form of oligonucleotides, or other genetic constructs" (*id.* at col. 22, ll. 6-10).

5. Uhr further discloses that the "preparation of vectors which incorporate nucleic acid sequences capable of encoding the desired genes, once introduced into the cells to be treated, is also contemplated. In this regard, replication defective retrovirus, such as LNSX, LN or N2A, may be used" (*id.* at col. 22, ll. 14-19).

6. Uhr further discloses that "[s]everal studies are contemplated to assay the effects of fos expression, and a variety of other protooncogenes, on malignant growth and cell cycle arrest, both in in vivo and in vitro" (*id.* at col. 22, ll. 43-45).

7. Uhr discloses, for example, that "[t]ransfected clones will be introduced into normal Balb/c and Id-immune mice, in controlled

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[3] Substitute Specification filed June 3, 2002.

experiments, and malignant growth [will] be evaluated" (*id.* at col. 22, ll. 48-50).

8. Uhr discloses that "it will be important to demonstrate the presence of cell cycle arrested tumor cells. Spleen from mice >60 days after tumor cell transplant will be analyzed for arrested BCL_1 cells by FACS, employing the methods of the present invention" (*id.* at col. 22, ll. 56-60).

9. Uhr discloses that, using its FACS cell sorting methods, "cells can be sperated [sic] on the basis of 6 parameters" (*id.* at col 3, ll. 64-65).

10. Conneally discloses studies of retroviral transfection of "primary human hematopoietic cell targets using an amphotropic vector encoding heat-stable antigen (HSA) . . . as a selectable marker" (Conneally 457).

11. Conneally discloses:

> These studies highlight the potential of using retroviral constructs encoding cell surface markers not normally expressed on the target cells of interest to facilitate the selection immediately after infection of those to which gene transfer has been achieved. For many gene therapy applications, the capacity to control the number or proportion of transduced stem cells could be of considerable significance . . . .

(Conneally 462.)

12. Thus, Conneally discloses, "[o]ne of the major advantages of the HSA/CD24 family of vectors is the ability to assess gene transfer to specific subpopulations of cells immediately after infection" (*id.*)

PRINCIPLES OF LAW

In *KSR Int' l Co. v. Teleflex Inc.*, 550 U.S. 398 (2007), the Supreme Court advised that, in determining whether the prior art supplied a reason for practicing the claimed subject matter, the analysis "need not seek out precise teachings directed to the specific subject matter of the challenged claim, for

a court can take account of the inferences and creative steps that a person of ordinary skill in the art would employ." *Id.* at 418; *see also id.* at 421 ("A person of ordinary skill is . . . a person of ordinary creativity, not an automaton.").

The Court also reasoned that "[i]n determining whether the subject matter of a patent claim is obvious, neither the particular motivation nor the avowed purpose of the patentee controls. What matters is the objective reach of the claim. If the claim extends to what is obvious, it is invalid under § 103." *Id.* at 419.

Lastly, during examination, the PTO must interpret terms in a claim using "the broadest reasonable meaning of the words in their ordinary usage as they would be understood by one of ordinary skill in the art, taking into account whatever enlightenment by way of definitions or otherwise that may be afforded by the written description contained in the applicant's specification." *In re Morris*, 127 F.3d 1048, 1054 (Fed. Cir. 1997).

ANALYSIS

We agree with the Examiner that the evidence of record supports a finding that the cited references suggest a process that includes a step of "providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents" as recited in claim 17.

The Specification defines a "population of cells" or "library of cells" or "plurality of cells" as meaning "at least two cells" (Spec. 9 (FF 2)). Given this definition, we further agree with the Examiner that the population of retroviral-transfected cells suggested by Uhr, which would include at least two retroviral vectors (one encoding c-fos, the other encoding c-jun), would

be encompassed by the "population of cells comprising a library of retroviral vectors" recited in claim 17.

Turning to the prior art, Uhr discloses processes of treating cancer by arresting tumor cells' growth cycle (FF 3-4). Uhr discloses that cell cycle-arresting genes, such as c-fos and c-jun can be introduced into cells using retroviruses (FF 4-5). Uhr further discloses that the effect of the genes encoded by the retroviruses can be studied by implanting the gene-carrying cells into mice, and then removing presumed cycle-arrested cells from the mice and sorting them by FACS, using as many as 6 parameters, to evaluate the presence of the altered cell cycle phenotype (FF 6-9).

In view of these teachings, we agree with the Examiner that Uhr would have suggested to an ordinary artisan that it would be desirable to transfect a population of cells with retroviral vectors encoding at least two potential cell cycle-arresting genes, c-fos and c-jun. As pointed out by the Examiner, Conneally also discloses the desirability of using retroviral vectors having detectable cell surface markers as vehicles for nucleic acids of interest (FF 10-12).

We acknowledge, as Appellants argue, that Uhr refers to its methods as "gene therapy" (FF 4). Regardless of terminology, however, given Uhr's teachings, we find that Uhr would have prompted an ordinary artisan to provide a population of cells including at least two different retroviral vectors encoding tumor cell cycle-arresting agents, one encoding c-fos, the other encoding c-jun.

In sum, we agree with the Examiner that an ordinary artisan viewing the teachings of the cited references have been prompted to transfect a population of cells with retroviral vectors encoding at least two potential cell

cycle-arresting genes, c-fos and c-jun. As claim 17 encompasses a library of this size, we conclude that the evidence of record supports the Examiner's position that the cited references suggest performing claim 17's step of "providing a population of cells comprising a library of retroviral vectors encoding different candidate bioactive agents."

Accordingly, we affirm the Examiner's obviousness rejection of claim 17 over Uhr and Conneally, as well as the rejection of claims 18-24 and 30, which were not argued separately. *See* 37 C.F.R. § 41.37(c)(1)(vii).

OBVIOUSNESS -- NOLAN, JAI-PING AND UHR

ISSUE

Claims 17-25, 30, and 32 stand rejected under 35 U.S.C. § 103(a) as obvious over Nolan, Jia-ping, and Uhr (Ans. 7-10).

In traversing this rejection, Appellants do not dispute the Examiner's fact findings regarding the references' teachings or the conclusions drawn from them. Rather, Appellants argue only that the Nolan reference is not prior art with respect to the instant application as evidenced by the Fisher Declaration (App. Br. 7-9).

Specifically, Appellants argue, the instant application claims priority to an application (09/062,330) filed less than one year after the publication date of the Nolan reference, and the Nolan reference is therefore available as prior art to the instant application only under 35 U.S.C. § 102(a) (*id.* at 8). Thus, Appellants urge, because the Fisher Declaration filed under 37 C.F.R. § 1.131 establishes invention of the subject matter in the rejected claims prior to the publication date of Nolan, Nolan is not available as prior art against the rejected claims (*id.*). Appellants further urge that the Examiner has failed to properly consider the Fisher Declaration (*id.*)

The Examiner responds that "Nolan was published more than one year [before] applicants' earliest filing date (please note appellants' statement that the instant application is a continuation-in-part (CIP) of the 09/062,330 application)" (Ans. 17). *See also* Final Rejection 13 (entered August 10, 2007) ("[T]he 35 USC 1.131 declaration does not overcome the 103 rejection *based on 102(b)* rejection over the Nolan reference as Nolan (WO 97/27212) *is a bar* against the instant application.") (Emphasis added).

Specifically, the Examiner urges, Appellants "are not entitled to the priority date of the '330 application" because the '330 application does not provide support for screening for "'at least five parameters,'" and also does not provide support for screening for all of the phenotypes recited in the rejected claims (Ans. 17).

In view of the positions advanced by Appellants and the Examiner, the issue with respect to this rejection is whether Appellants are entitled to priority to parent application serial no 09/062,330, which issued as U.S. Patent 6,897,031.

PRINCIPLES OF LAW

37 C.F.R. § 1.131 states, in relevant part (emphasis added):

> (a) When any claim of an application or a patent under reexamination is rejected, the inventor of the subject matter of the rejected claim, the owner of the patent under reexamination, or the party qualified under §§ 1.42, 1.43, or 1.47, may submit an appropriate oath or declaration to establish invention of the subject matter of the rejected claim prior to the effective date of the reference or activity on which the rejection is based. . . . Prior invention *may not be established* under this section if . . .
>
> (2) The rejection is based on a statutory bar.

Thus, a declaration under 37 C.F.R. § 1.131 cannot overcome a rejection for anticipation or obviousness where the prior art antedates the application's effective filing date by more than one year, and is therefore applicable against the claims under 35 U.S.C. § 102(b). *See In re Foster*, 343 F.2d 980, 989-90 (CCPA 1965).

Accordingly, for Appellants to overcome the statutory bar set by § 102(b), Appellants' claimed subject matter must find support in Application Serial No. 09/062,330, filed on April 17, 1998, which issued as U.S. Patent No. 6,897,031 B1 (*see* FF 16, *below*).

"[T]he test to determine if an application is to receive the benefit of an earlier filed application is whether a person of ordinary skill in the art would recognize that the applicant possessed what is claimed in the later filed application as of the filing date of the earlier filed application." *Noelle v. Lederman*, 355 F.3d 1343, 1348 (Fed. Cir. 2004).

Thus, to receive benefit of a previous application, *every feature* recited in the claims at issue must be described in the prior application. *See In re van Langenhoven*, 173 USPQ 426, 429 (CCPA 1972) ("The fact that *some* of the elements of the breech claims have support of the parent and foreign applications does not change the result. *As to given claimed subject matter, only one effective date is applicable.*") (Emphasis added); *accord In re Chu*, 66 F.3d 292, 297 (Fed. Cir. 1995).

FINDINGS OF FACT ("FF")

13. It is undisputed that the publication date of the Nolan reference is July 31, 1997.

14. The filing date of the instant application is April 16, 1999 (*see* Transmittal of New Application (entered April 16, 1999)), which is more than one year after the publication date of the Nolan reference.

15. The Specification states that "[t]his application is a continuation-in-part of U.S. Application Serial No. 09/062,330, filed on April 17, 1998 [now U.S. Patent No. 6,897,031 B1], and U.S. Application Serial No. 09/157,748, filed on September 21, 1998 (Specification 1 (as amended September 24, 2004)).

16. Thus, to remove the statutory bar set by 35 U.S.C. § 102(b) against patenting claims anticipated or obviated by printed publications available more than one year prior to an application's filing date, Appellants' claimed subject matter must find support in Application Serial No. 09/062,330, filed on April 17, 1998, which issued as U.S. Patent No. 6,897,031 B1.

17. The Examiner finds:

> The 09/062330 (now US Patent 6,897,031) ('031 Patent) does not provide support for the present broad claim "at least 5 parameters" as applied to the different claim cellular phenotypes. The different claim phenotypes consist of cell cycle, apoptosis, exocytosis, expression of a cell surface receptor, and expression of a receptor protein. The '031 Patent provides only four (4) parameters solely for exocytosis. It does not provide support for the other claim cell phenotypes having "at least five (5)" parameters being determined. See e.g., Example 9 of the '031 Patent.

(Ans. 17.)

18. Appellants do not dispute the Examiner's characterization of the disclosure of the '330 application/'031 patent.

19. The '031 patent states:

> Described is a method for screening for alterations in exocytosis of a population of cells. The cells are sorted by a FACS machine by assaying for alterations in at least three of the properties selected from the group consisting of light scattering, fluorescent dye uptake, fluorescent dye release, annexin granule binding, surface granule enzyme activity, and the quantity of granule specific proteins. Methods for screening for bioactive agents capable of modulating exocytosis in a cell are also described. The methods provide for reduced background and increased specificity without increasing the time or steps involved in assaying for exocytosis.

('031 patent, abstract).

20. Appellants do not point to any disclosure in the '031 patent regarding sorting cells based on at least five parameters as recited in step (b) of claim 17. Nor do Appellants point to any disclosure of screening for alterations in all of the cellular phenotypes recited in the "wherein" clause of claim 17.

ANALYSIS

We agree with the Examiner that Appellants have not shown that the Nolan reference is unavailable as prior art against the rejected claims. As noted above, Appellants cannot avail themselves of an antedating declaration under 37 C.F.R. § 1.131 if the rejection is a statutory bar. *See In re Foster*, 343 F.2d at 989-90.

Thus, to avoid the statutory bar set by 35 U.S.C. § 102(b), Appellants must find descriptive support for the rejected claims in a priority application filed less than one year after publication of the Nolan reference. In the instant case, only the '330 application, which issued as the '031 patent, and which is asserted as a continuation-in-part parent to this application, has such a filing date (*see* FF 15).

However, as the Examiner points out, and Appellants do not dispute, the '330 application/'031 patent does not describe all of the features in the rejected claims (FF 17-20). Thus, given the evidence of record, the earliest effective filing date of the instant application is April 16, 1999, which is more than one year after the Nolan reference's publication date of July 31, 1997 (FF 13-14). Accordingly, the Fisher Declaration under 37 C.F.R. § 1.131 cannot be used to antedate the Nolan reference.

We therefore agree with the Examiner that Nolan is available prior art against the rejected claims. As Appellants' sole argument was on this basis, and as we detect no other deficiency in the Examiner's case of obviousness, we affirm the Examiner's obviousness rejection of claims 17-25, 30, and 32 over Nolan, Jia-ping, and Uhr.

The Examiner also rejected claim 26 as obvious over Nolan, Jia-ping, Uhr, Hide, and Appellants' admitted prior art (Ans. 10-11). Appellants' sole argument against this rejection is also the unavailability of Nolan as prior art against the rejected claim (App. Br. 9). As discussed above, we do not find this argument persuasive. We therefore also affirm this rejection.

SUMMARY

We affirm the Examiner's obviousness rejection of claims 17-24 and 30 over Uhr and Conneally.

We also affirm the Examiner's obviousness rejection of claims 17-25, 30, and 32, over Nolan, Jia-ping, and Uhr.

We also affirm the Examiner's obviousness rejection of claim 26 over Nolan, Jia-ping, Uhr, Hide, and Appellants' admitted prior art.

TIME PERIOD

No time period for taking any subsequent action in connection with this appeal may be extended under 37 C.F.R. § 1.136(a).

AFFIRMED

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